REPLACED BY ART 34 AMDT

PATENT COOPERATION TREATY

PCT

RECD 11 APR 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
HL 71375/002		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/00673	24/02/2000	04/03/1999
International Patent Classification (IPC) or national classification and IPC C07C41/09		
Applicant THOMAS SWAN & CO. LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of ~~8~~ 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
20/09/2000	09.04.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Lorenzo, M.J. Telephone No. +49 89 2399 8239

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00673

I. Basis of the report

1. With regard to the **lements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-4, 6-15 as originally filed
5, 5a received on 14.03.01 filed with letter of 12.03.0

Claims, No.:

1-16 received on 14.03.01 filed with letter of 12.03.0

Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
see separate sheet

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-16
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-16
Industrial applicability (IA)	Yes:	Claims	1-16
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

R It m I

Basis of the report

The amendments submitted by the applicant with his letter dated 12.03.01 do not fulfil the requirements of Article 19(2) PCT. The amendments on claim 1 and on page 5 of the description changing "under supercritical or near-critical conditions" by "under supercritical or near-critical conditions for the fluid that is acting as solvent" are considered to go beyond the disclosure as filed (Rule 70.2(c)). Therefore, the establishment of opinion with regard to novelty, inventive step and industrial applicability is based on the application as originally filed.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1: US-A-5 831 116

The present application relates to a method for producing ether, acetal, ketal or alkene derivatives which comprises reacting an alcohol in the presence of a heterogeneous acid catalyst under supercritical or near critical conditions.

The closest prior art, document D1, discloses a method for partially oxidising alcohols which comprises a)introducing into a reactor unit containing a bed of solid acid catalyst (Lewis acid), an alcohol, oxygen and a supercritical fluid (such as CO_2 or N_2) mobile phase; and b)partially oxidising the alcohol to its corresponding ether, aldehyde, ester or acid, wherein the operating pressure and temperature are greater than the critical point pressure and temperatures of the mixture of alcohol, oxygen and the supercritical fluid.

The disclosure of D1 anticipates thus the subject-matter of claims 1-16 of the present application which are, therefore, not novel according to Article 33(2) PCT. The objection raised in the previous communication against the subject-matter of the application for lack of novelty is, despite the arguments brought forward in the Applicant's letter of reply, maintained.

Re It m VI

Certain documents cited

Although the document J. Am. Chem. Soc. published on 11.06.99 is not considered to be part of the prior art in the sense of Rule 64.1 PCT for the purposes of Articles 33(2) and (3) PCT, this document (see abstract and tables 2-6) would anticipate the subject-matter of the claims of the present application if the priority date of the latter is not valid. This document could become very relevant to assess the patentability of the present application when it enters the national/regional phase. No check has been made as to whether the priority of the present application has been validly claimed.

Re Item VII

Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description, nor is this document identified therein.

2. The units of pressure "atm" employed in examples 4-8 are not additionally expressed in terms of the units stipulated by Rule 10.1/(a)/and/(b) PCT.

Re Item VIII

Certain observations on the international application

1. Claims 11 and 15 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not defined. The claims attempt to define the subject-matter in terms of the result to be achieved. In this instance, such a formulation is not allowable because it appears possible to define the subject-matter in more concrete terms, viz. in terms of how the effect is to be achieved.

2. Features introduced by "preferred" in claim 2 have no limiting effect on the scope of the claim (see PCT Guidelines, C-IV, 4.6). The presence of such non-limiting features is however detrimental to the conciseness of the claim, contrary to Art. 6 PCT.

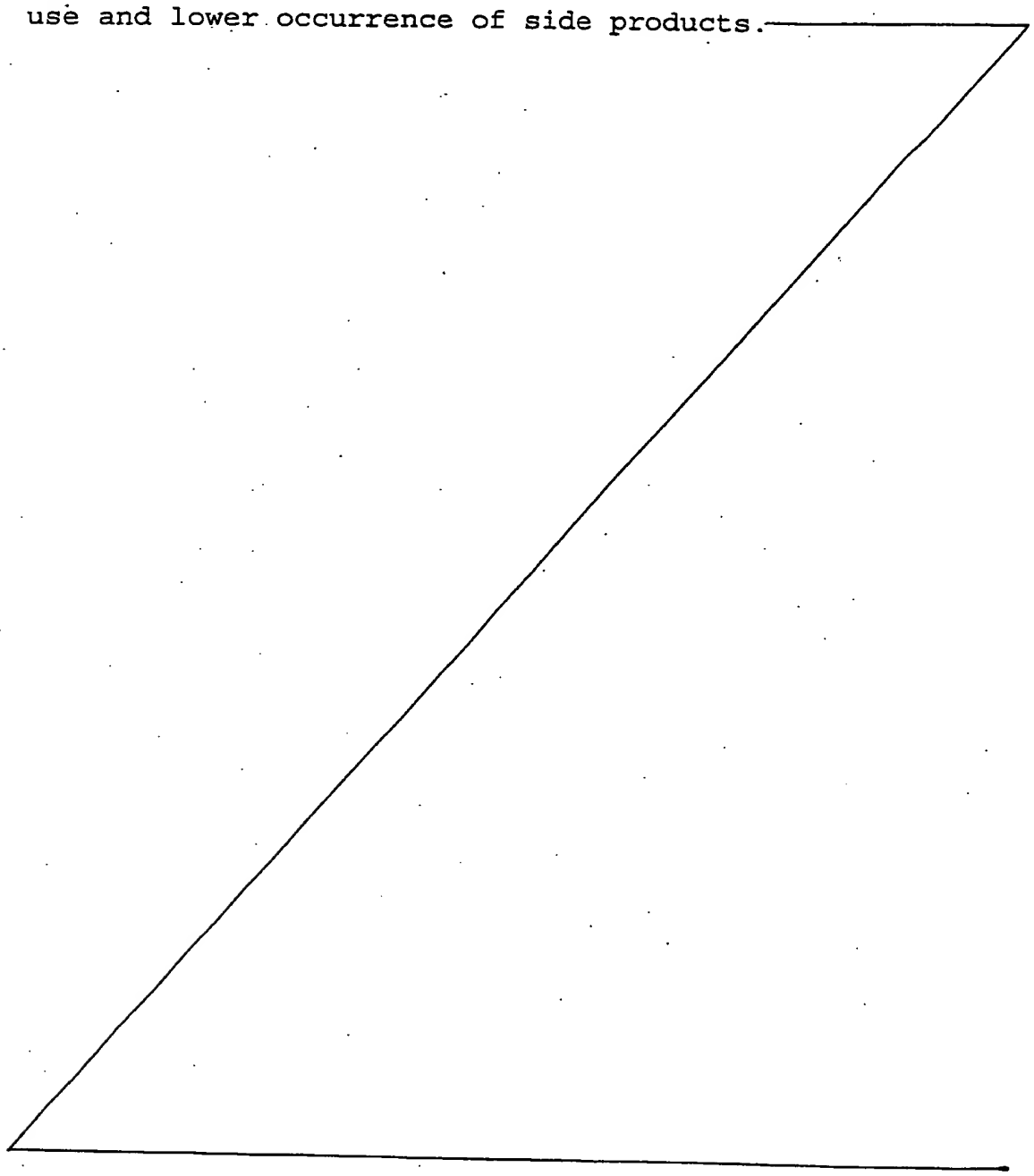
One consequence of using the heterogeneous catalyst is that there is no need for complicated separation procedures to liberate the product from the reaction mixture and catalyst. This represents quite a benefit in terms of both the time savings and cost savings of the present invention.

We have thus found that it is possible by using a combination of supercritical fluids and a heterogeneous catalyst (e.g. the Deloxan ASP catalyst from Degussa or Acidic Amberlyst resin from Rohm and Haas) in a continuous flow reactor to carry out a number of reactions rapidly and cleanly. These reactions can often be performed in high yield and take place under near-critical or supercritical conditions.

According to the present invention, there is provided A process in which a hydroxyl-substituted organic compound selected from the formulae R_1CH_2OH, R^1R^2CHOH and $R^1R^2R^3COH$ is exposed, optionally in the presence of one or more further organic compounds selected from second hydroxyl-substituted organic compounds of the formulae R^4CH_2OH, R^5R^6CHOH, and $R^7R^8R^9COH$ and carbonyl compounds of the formula $R^{10}R^{11}CO$, to a heterogeneous catalyst which is able to provide a source of acid in a continuous flow reactor under supercritical conditions or at near-critical conditions for the fluid that is acting as solvent, with the result that an ether is formed from two hydroxyl-substituted organic compound molecules in a dehydration reaction, an acetal or ketal is formed by reaction between a hydroxyl-substituted organic compound molecule and a molecule of a said carbonyl compound and an alkene product is produced by dehydration of a single hydroxyl-substituted organic compound molecule, wherein the conditions of temperature, pressure, and flow rate are controlled according to the product to be obtained, and wherein each of R^1 to R^{11} is independently

selected from: hydrogen or hydroxyl; an optionally substituted alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, cycloalkenyl, or aryl; or a heterocyclic group.

Aliphatic and aromatic alcohols are preferred because they give cleaner reactions, with aliphatic alcohols being most preferred on the grounds of ease of use and lower occurrence of side products.



Claims

1. A process in which a hydroxyl-substituted organic compound selected from the formulae R_1CH_2OH, R^1R^2CHOH and $R^1R^2R^3COH$ is exposed, optionally in the presence of one or more further organic compounds selected from second hydroxyl-substituted organic compounds of the formulae R^4CH_2OH, R^5R^6CHOH, and $R^7R^8R^9COH$ and carbonyl compounds of the formula $R^{10}R^{11}CO$, to a heterogeneous catalyst which is able to provide a source of acid in a continuous flow reactor under supercritical conditions or at near-critical conditions for the fluid that is acting as solvent, with the result that an ether is formed from two hydroxyl-substituted organic compound molecules in a dehydration reaction, an acetal or ketal is formed by reaction between a hydroxyl-substituted organic compound molecule and a molecule of a said carbonyl compound and an alkene product is produced by dehydration of a single hydroxyl-substituted organic compound molecule, wherein the conditions of temperature, pressure, and flow rate are controlled according to the product to be obtained, and wherein each of R^1 to R^{11} is independently selected from: hydrogen or hydroxyl; an optionally substituted alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, cycloalkenyl, or aryl; or a heterocyclic group.

2. A process according to claim 1, wherein each of R^1 to R^{11} when present is an optionally substituted alkyl group.

3. A process according to claim 2, wherein each of the alkyl groups independently contains not more than 10 carbon atoms in the carbon chain (excluding optional substituents if present).

4. A process according to claim 1, 2 or 3, wherein the total number of alcohol groups within the organic compound does not exceed three.

5. A process according to any preceding claim, wherein the reaction is performed under supercritical conditions.

6. A process according to any preceding claim, wherein the organic compound of formula R^1CH_2OH, R^1R^2CHOH or $R^1R^2R^3COH$, and optionally one or more of the compounds of formulae R^4CH_2OH, R^5R^6CHOH, $R^7R^8R^9COH$ or $R^{10}R^{11}CO$, is dissolved in a fluid selected from: carbon dioxide, propane, an alkene, an alkyne, hydrocarbon, halocarbon, nitrogen, or a mixture of any of these.

7. A process according to any one of claims 1 to 5, wherein the organic compound is the supercritical or near-critical fluid.

8. A process according to any preceding claim, wherein the catalyst is selected from: zeolites, metal oxides, molecular sieves, clays, or sulfonic acid derivatives.

9. A process according to claim 8, wherein the catalyst is supported on an inert carrier.

10. A process according to claim 8 or 9, wherein the catalyst includes a promoter.

11. A process according to any of claims 8, 9 or 10, wherein the acidity of the catalyst is provided by a sulfonic acid group.

12. A process according to any preceding claim, wherein the reactant molecules are aliphatic and/or aromatic alcohols.

13. A process according to any preceding claim, in which the product is an ether.

14. A process according to claim 13, in which the reactant(s) and the product are straight-chain n-alkyl molecules.

15. A process according to claim 11 or 12, wherein an aliphatic alcohol is converted into an alkene.

16. A process according to any preceding claim, in which the reactant(s) form a single homogeneous phase.

One consequence of using the heterogeneous catalyst is that there is no need for complicated separation procedures to liberate the product from the reaction mixture and catalyst. This represents quite a benefit in terms of both the time savings and cost savings of the present invention.

We have thus found that it is possible by using a combination of supercritical fluids and a heterogeneous catalyst (e.g. the Deloxan ASP catalyst from Degussa or Acidic Amberlyst resin from Rohm and Haas) in a continuous flow reactor to carry out a number of reactions rapidly and cleanly. These reactions can often be performed in high yield and take place under near-critical or supercritical conditions.

According to the present invention, there is provided a process in which an organic compound having the formula R^1CH_2OH, R^1R^2CHOH, or $R^1R^2R^3COH$ is exposed, optionally in the presence of one or more further organic compounds having the formula R^4CH_2OH, R^5R^6CHOH, $R^7R^8R^9COH$ or $R^{10}R^{11}CO$, to a heterogenous catalyst which is able to provide a source of acid in a continuous flow reactor under supercritical or near-critical conditions with the result that an ether, acetal, ketal or alkene product is formed, wherein the conditions of temperature, pressure, and flow rate are independently controlled, and wherein each of R^1 to R^{11} is independently selected from: hydrogen, hydroxyl, or an optionally substituted alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, cycloalkenyl, aryl or heterocyclic group.

Aliphatic and aromatic alcohols are preferred because they give cleaner reactions, with aliphatic alcohols being most preferred on the grounds of ease of use and lower occurrence of side products.

Claims

1. A process in which an organic compound having the formula R^1CH_2OH, R^1R^2CHOH or $R^1R^2R^3COH$ is exposed, optionally in the presence of one or more further organic compounds having the formulae R^4CH_2OH, R^5R^6CHOH, $R^7R^8R^9COH$ or $R^{10}R^{11}CO$, to a heterogeneous catalyst which is able to provide a source of acid in a continuous flow reactor under supercritical or near-critical conditions with the result that an ether, acetal, ketal or alkene product is formed, wherein the conditions of temperature, pressure, and flow rate are independently controlled, and wherein each of R^1 to R^{11} is independently selected from: hydrogen or hydroxyl; an optionally substituted alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, cycloalkenyl, or aryl; or a heterocyclic group.

2. A process according to claim 1, wherein each of R^1 to R^{11} when present is an optionally substituted alkyl group, preferably each of the alkyl groups independently containing not more than 10 carbon atoms in the carbon chain (excluding optional substituents if present).

3. A process according to claim 1 or 2, wherein the total number of alcohol groups within the organic compound does not exceed three.

4. A process according to claim 1, 2 or 3, wherein the reaction is performed under supercritical conditions.

5. A process according to any preceding claim, wherein the organic compound of formula R^1CH_2OH, R^1R^2CHOH or $R^1R^2R^3COH$, and optionally one or more of the compounds of formulae R^4CH_2OH, R^5R^6CHOH, $R^7R^8R^9COH$ or $R^{10}R^{11}CO$, is dissolved in a fluid selected from: carbon dioxide, propane, an alkene, an alkyne, hydrocarbon, halocarbon, nitrogen, or a mixture of any of these.

6. A process according to claim 1, 2, 3 or 4, wherein the organic compound is the supercritical or near-critical fluid.

7. A process according to any preceding claim, wherein the catalyst is selected from: zeolites, metal oxides, molecular sieves, clays, or sulfonic acid derivatives.

8. A process according to claim 7, wherein the catalyst is supported on an inert carrier.

9. A process according to claim 7 or 8, wherein the catalyst includes a promoter.

10. A process according to any of claims 7, 8 or 9, wherein the acidity of the catalyst is provided by a sulfonic acid group.

11. A process according to any preceding claim, wherein the reaction conditions are controlled in such a way that the products are selectively formed in high yield with insignificant rearrangement.

12. A process according to claim 11, wherein the reactant molecules are aliphatic and/or aromatic alcohols, preferably aliphatic alcohols.

13. A process according to any preceding claim, in which the product is an ether.

14. A process according to claim 13, in which the reactant(s) and the product are straight-chain n-alkyl molecules.

15. A process according to claim 11 or 12, wherein the reaction conditions can be controlled in such a way that a particular alcohol is converted into an alkene in preference to an ether.

16. A process according to any preceding claim, in which the reactant(s) form a single homogeneous phase.